(PCT Article 18 and Rules 43 and 44)

International application No.	Applicant's or agent's file reference 01-0834EP 05	FOR FURTHER see Notification of Transmittal of International Search Report (Form PCT/ISA/220) as well as, where applicable, item 5 below.						
INSTITUTO SUPERIOR T CNICO et a1. This international Search Report has been prepared by this international Searching Authority and is transmitted to the applicant according to Article 16. A copy is being transmitted to the international Bureau. This International Search Report consists of a total of		International filing date (day/month/year)	(Earliest) Priority Date (day/month/year)					
This international Search Report has been prepared by this International Searching Authority and is transmitted to the applicant according to Article 16. A copy is being transmitted to the international Bureau. This International Search Report consists of a total of	PCT/PT 01/00008	00008 17/05/2001 17/05/2000						
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This International Search Report consists of a total of	INSTITUTO SUPERIOR T CNIC	O et al.						
It is also accompanied by a copy of each prior art document cited in this report. 1. Basis of the report a. With regard to the language, the international search was carried out on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item. the international search was carried out on the basis of a translation of the international application furnished to this Authority (Fulle 23.1(b)). With regard to any nucleotide and/or amino acid sequence disclosed in the international application, the international search was carried out on the basis of the sequence listing: contained in the international application in written form. filled together with the international application in computer readable form. furnished subsequently to this Authority in written form. furnished subsequently to this Authority in computer readable form. furnished subsequently to this Authority in computer readable form. the statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished. the statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished. Unity of invention is lacking (see Box II). Unity of invention is lacking (see Box II). With regard to the title, the text is approved as submitted by the applicant. The text has been established by this Authority to read as follows: PROCESS FOR THE CONTINUOUS PRODUCTION OF DIPEPTIDE CRYSTALS IN A MEMBRANE AND HYDRO-CYCLONE RACTOR USING A PEPTIDASE 5. With regard to the abstract, the text has been established, according to the international search report, submit comments to this Authority, within one month from the date of mailing of this international search report, submit comments to this Authority. A submit of the date of mailing of this international search report, submit comments to this Authority.			hority and is transmitted to the applicant					
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International application No. PCT PT 01/00008

Box III TEXT OF THE ABSTRACT (Continuation of item 5 of the first sheet)

The invention relates to a process for the production of dipeptide crystals (generic formula AcXYNH2) with high purity (>95%), by enzymatic synthesis with a protease in organic media of reversed micelles, starting from derivatives of the two constituent amino acids)AcXOEt and YNH2). A membrane and hydro-cyclone reactor was designed which enables the continuous and simultaneous synthesis and crystallisation of the dipeptides. The dipeptide crystals thus prepared are continuously removed and further separated from the remaining liquid by filtration or centrifugation. After drying, the crystals are dissolved in hot methanol. By decreasing the temperature, the dipeptide re-crystallises, originating a high purity product. After re-crystallisation the product is filtered and dried.

PCT 01/00008

A. CLASSIFICATION OF SUBJECT MATTER IPC 7 C12P21/02 C07K C07K1/36 C07K1/02 C12M1/12 ·B04C3/00 According to International Patent Classification (IPC) or to both national classification and IPC B. FIELDS SEARCHED Minimum documentation searched (classification system followed by classification symbols) C12P C07K C12M BO4C Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched Electronic data base consulted during the international search (name of data base and, where practical, search terms used) C. DOCUMENTS CONSIDERED TO BE RELEVANT Category 6 Citation of document, with indication, where appropriate, of the relevant passages Relevant to claim No. χ SERRALHEIRO M L M ET AL: "Continuous $\frac{1}{2}$,2,4,5, production and simultaneous precipitation of a dipeptide in a reversed micellar membrane reactor." ENZYME AND MICROBIAL TECHNOLOGY. vol. 24, no. 8-9, June 1999 (1999-06), pages 507-513, XP001010232 ISSN: 0141-0229 cited in the application Υ the whole document 3,6 Y FR 2 679 235 A (AJINOMOTO KK) 3,6 22 January 1993 (1993-01-22) the whole document -/--Further documents are listed in the continuation of box C. Patent family members are listed in annex. ° Special categories of cited documents: 'T' later document published after the international filing date or priority date and not in conflict with the application but 'A' document defining the general state of the art which is not considered to be of particular relevance cited to understand the principle or theory underlying the invention earlier document but published on or after the international "X" document of particular relevance; the claimed invention filing date cannot be considered novel or cannot be considered to 'L' document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another involve an inventive step when the document is taken alone "Y" document of particular relevance; the claimed invention citation or other special reason (as specified) cannot be considered to involve an inventive step when the document is combined with one or more other such docu-"O" document referring to an oral disclosure, use, exhibition or other means ments, such combination being obvious to a person skilled document published prior to the international filing date but later than the priority date claimed in the art. "&" document member of the same patent family Date of the actual completion of the international search Date of mailing of the international search report 6 July 2001 17/07/2001 Name and mailing address of the ISA Authorized officer European Patent Office, P.B. 5818 Patentlaan 2 NL - 2280 HV Rijswijk Tel. (+31-70) 340-2040, Tx. 31 651 epo nl, Smalt, R Fax: (+31-70) 340-3016

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International Application No PCT 01/00008

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x /	FELICIANO A S ET AL: "The effect of stirring and seeding on the AcPheLeuNH2 synthesis and crystallization in a reversed micellar system." ENZYME AND MICROBIAL TECHNOLOGY, vol. 27, no. 3-5, August 2000 (2000-08), pages 264-269, XP001010217 ISSN: 0141-0229 cited in the application the whole document	1,2,4,5,			
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A	FELICIANO A S ET AL: "Quantitative structure activity relationships in the synthesis of AcXYNH-2 dipeptides by alpha-chymotrypsin in reversed micelles." ENZYME AND MICROBIAL TECHNOLOGY, vol. 21, no. 4, 1997, pages 284-290, XP001010223 ISSN: 0141-0229 cited in the application the whole document				

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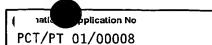
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International Application No
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A. CLASSIFICATION OF SUBJECT MATTER IPC 7 C12P21/02 C07K1/36 C07K1/02 C12M1/12 B04C3/00 According to International Patent Classification (IPC) or to both national classification and IPC **B. FIELDS SEARCHED** Minimum documentation searched (classification system followed by classification symbols) C12P CO7K C12M B04C Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched Electronic data base consulted during the international search (name of data base and, where practical, search terms used) C. DOCUMENTS CONSIDERED TO BE RELEVANT Category 5 Citation of document, with indication, where appropriate, of the relevant passages Relevant to claim No. X SERRALHEIRO M L M ET AL: "Continuous 1,2,4,5, production and simultaneous precipitation of a dipeptide in a reversed micellar membrane reactor." ENZYME AND MICROBIAL TECHNOLOGY, vol. 24, no. 8-9, June 1999 (1999-06), pages 507-513, XP001010232 ISSN: 0141-0229 cited in the application Υ the whole document 3,6 Υ FR 2 679 235 A (AJINOMOTO KK) 3,6 22 January 1993 (1993-01-22) the whole document Further documents are listed in the continuation of box C. Patent family members are listed in annex. Special categories of cited documents: *T* later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the theory. "A" document defining the general state of the art which is not considered to be of particular relevance invention *E* earlier document but published on or after the international "X" document of particular relevance; the claimed invention filing date cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified) "Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such docu-"O" document referring to an oral disclosure, use, exhibition or ments, such combination being obvious to a person skilled document published prior to the international filing date but later than the priority date claimed in the art. "&" document member of the same patent family Date of the actual completion of the international search Date of mailing of the international search report 6 July 2001 17/07/2001 Name and mailing address of the ISA Authorized officer European Patent Office, P.B. 5818 Patentlaan 2 NL - 2280 HV Rijswijk Tel. (+31-70) 340-2040, Tx. 31 651 epo nl, Fax: (+31-70) 340-3016 Smalt, R

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